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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/261,329	03/03/1999	KIM VILBOUR ANDERSEN	4887.204-US	7632

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EXAMINER

SLOBODYANSKY, ELIZABETH

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 10/03/2003

23

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/261,329

Applicant(s)

ANDERSEN ET AL.

Examiner

Elizabeth Slobodyansky

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 May 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 148-203 is/are pending in the application.
- 4a) Of the above claim(s) 149-182, 184-196, 199 and 201 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 148, 183, 197, 198, 200 and 202 is/are rejected.
- 7) ☒ Claim(s) 203 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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DETAILED ACTION

The amendment filed May 5, 2003 (Paper No. 22) canceling claims 79-147 and adding claims 148-203 has been entered.

Claims 148-203 are pending.

Election/Restriction

Applicant's election with traverse of cellulase of SEQ ID NO:5 mutated at a position corresponding to position 119 in SEQ ID NO:1 in Paper No. 22 is acknowledged. The traversal is on the ground(s) that "there would not be a serious burden on the examiner if election of species were not required. All of the species are classified in the same class and subclass. Furthermore, the same prior art has to be considered in determining patentability of each species" (Remarks, page 9). This is not found persuasive because while the species are classified in the same class and subclass each of the recited position would require a separate search and consideration.

The requirement is still deemed proper and is therefore made FINAL.

Applicant did not indicate which of the added claims are readable upon the elected species as required by MPEP § 809.02(a).

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Currently, claims 148 and 200 are generic. Claims 183, 197, 198, 202 and 203 correspond to the elected invention of SEQ ID NO:5 mutated at position corresponding to position 119 in SEQ ID NO:1.

Claims 149-182, 184-196, 199 and 201 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 148, 183, 197, 200 and 202 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 148 is directed to a genus of cellulases of SEQ ID NOs : 1-11 having endoglucanase activity comprising one or more mutations at the specific positions corresponding to positions of SEQ ID NO:1. Because "comprising " is open language and "one or more" does not limit the number of mutations, the claim does not impose

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any structural limitations and reads on any structure that is not necessarily homologous with SEQ ID NO:1 or SEQ ID NO:5.

Claims 183, 197 and 202 are included in this rejection because of the use of "comprising" language that allows mutations in addition to the mutations at Q119.

These claims are directed to a genus of molecules exhibiting endoglucanase activity from any source. The specification teaches the structure of only two representative species of the endoglucanase from *Thielavia terrestris* having the sequence of SEQ ID NO: 5 with the single mutation Q119H or Q119D. The rest of the sequence, 200 amino acids, is identical to SEQ ID NO:5. However, the genus of modified endoglucanases comprises variants additionally mutated at any of said 200 amino acids. Therefore, many functionally and structurally unrelated proteins are encompassed within the scope of these claims, including partial amino acid sequences. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality. This is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

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Claims 148, 183, 197, 200 and 202 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a modified endoglucanase having the structure of SEQ ID NO: 5 mutated at a single position corresponding to residue 119 in SEQ ID NO:1, does not reasonably provide enablement for a modified endoglucanase of SEQ ID NO: 5 comprising said specific mutation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) considered in determining whether undue experimentation is required, are summarized the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claim 148 is directed to a genus of modified endoglucanases comprising one or more specific mutations. Because "comprising " is open language the claim does not impose any structural limitations and reads on any structure that is not necessarily

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homologous with SEQ ID NO: 5. Therefore, the breadth of these claims is much larger than the scope enabled by the specification.

The state of the art does not allow the predictability of the properties based on the structure. The specification does not teach which residues besides the specifically mutated are responsible for the resulting properties of the mutant. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of endoglucanases broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired properties/activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and amino acid sequence of a mutant with a substitution at a single position.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is

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unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not teach a rational and predictable scheme for modifying any residues in SEQ ID NO:5 with an expectation of obtaining the desired biological function that is exhibited by a disclosed mutant and the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Therefore, one skilled in the art would require guidance beyond that provided in the specification as to how to make a modified endoglucanase with the amino acid sequence of unknown homology to SEQ ID NO:5. Without such guidance, the experimentation left to those skilled in the art is undue.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 148, 183 and 200 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schulein et al. (A) in view of Schulein et al. (B).

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Claims 148, 183 and 200 are included in this 103 rejection to the extent that they clearly encompass the cellulase modified at a single position corresponding to residue 119 of SEQ ID NO:1. Thus both the 112 and 103 rejections are proper.

Schulein et al. (A) (US Patent 6,001,639, form PTO-892 mailed November 5, 2002) teach fungal endoglucanases from various sources including 43 kD endoglucanase from *Humicola insolens* DSM 1800 (column 3, lines 6-27, SEQ ID NO:1 in the instant application). They teach homology among endoglucanases (Figures 1 and 3). They disclose the sequence of endoglucanase from *Thielavia terrestris* (column 42, lines 58-62, SEQ ID NO:12) comprising the sequence of SEQ ID NO:5 of the instant invention.

Schulein et al. (B) (WO 94/07998, form PTO-1449 filed March 3, 1999) teach positions in a cleft comprising the catalytically active site, mutations of which will result in the improved enzymatic activity (page 20, lines 15-20, 29-35). They specifically teach position 119 in 43 kD endoglucanase from *Humicola insolens* DSM 1800 and homologous cellulases (page 21, lines 22-29).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a mutant of SEQ ID NO:5 taught by Schulein et al. (A) that is mutated at position corresponding to residue 119 of SEQ ID NO:1 as suggested by Schulein et al. (B). One skilled in the art would have been motivated to make such a mutant in order to obtain a modified endoglucanase with a different surface

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conformation of the catalytic cleft resulting in a different interaction pattern between an enzyme and a substrate.

However, one skilled in the art would have not expected that a specific mutation Q118H in SEQ ID NO:5 that corresponds to mutation at position 119 in SEQ ID NO:1 would result in about 3 fold increase of the enzymatic activity compared with the wild type endoglucanase of SEQ ID NO:5.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 198 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 198 is drawn to "the modified cellulase of claim 148, consisting of Q119H". The cellulase does not consists of a single amino acid. Amending the claim to recite "wherein a substitution in the parent cellulase consists of Q119H", for example, is suggested.

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Allowable Subject Matter

Claim 203 rewritten to be drawn to a mutant with a single mutation Q118H in SEQ ID NO:5 would be allowable. Q118H in SEQ ID NO:5 corresponds to Q119H in SEQ ID NO:1).

Response to Arguments

Applicant's arguments filed May 5, 2003 have been fully considered but they are not persuasive. .

With regard to the 112, 1st paragraph, rejection Applicants argue that "based on Applicants disclosure, the skilled artisan would be led to make other mutations in addition to the mutations recited in the claims to obtain the benefits described in the present application. Applicants therefore submit that the specification demonstrate that Applicants had possession of the claimed invention at the time the application was filed" (Remarks, page 9, penultimate paragraph). This is not persuasive because the number of said "other mutations in addition to the mutations recited in the claims" is not limited resulting in a structure that is not necessarily homologous to SEQ ID NO:1.

With regard to the 103(a) rejection, Applicants argue that "Schulein. (A) and Schulein (B) disclose various cellulases and variants thereof. However, neither Schulein et al. reference teaches or suggests the cellulase variants of the present invention" (page 10). This is not persuasive because as a secondary reference in the

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103(a) rejection, the Schulein et al. reference does not have to disclose the same invention but only to make it obvious. The combination of both references does suggest the invention for the reasons explained above.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

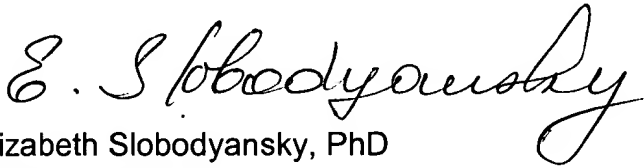
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

A handwritten signature in cursive script, reading "E. Slobodyansky". The signature is written in black ink and is positioned above the printed name and title.

Elizabeth Slobodyansky, PhD
Primary Examiner

September 30, 2003